R^6: a lower alkyl, -OH, -O-lower alkyl, -O-aryl which may have substituent(s), -O-lower alkylene-aryl which may have substituent(s), -NR^1-aryl which may have substituent(s), -CO-lower alkyl, or -aryl group which may have substituent(s); and

R^7: the same or different, H or the same group as R^6.

REMARKS

Entry and consideration of this Amendment is respectfully requested. Support for the amendments are as follows:

(1) The support for the changes from "3,4-$(CH)_4$" at page 35 and Tables to "3,4-(CH=CH-CH=CH)" is as follows. Please note that all changes in the Tables related to "3,4-$(CH)_4$".

At page 35, lines 17-19, it is described that "a compound in which R^2 is 3,4-$(CH)_4$ represents a 2-naphthyl group together with the adjacent benzene ring", which means that the description about "3,4-$(CH)_4$" means a naphthyl group. In order to further clarify that the definition means a naphthyl group, please change "3,4-$(CH)_4$" to "3,4-(CH=CH-CH=CH)". The compounds amended in this regard has 3,4-(CH=CH-CH=CH) as R^2.

(2) The support for the addition of "-OCH_2O-, or -(CH=CH-CH=CH)-" in Claim 1 and page 6, lines 23-24 is as follows.

The following compounds wherein R^2 is 2,3-OCH_2O or 3,4-OCH_2O are described.

Page 38, Table 3: Compound 34 and 35
Page 38, Table 4: Compound 70 and 71
Page 40, Table 6: Compound 154 and 155
Page 40, Table 7: Compound 190 and 191
Page 42, Table 9: Compound 274 and 275
Page 42, Table 10: Compound 310 and 311

The following compounds wherein R^2 is 3,4-(CH=CH-CH=CH) (i.e., 3,4-$(CH)_4$" before amendments) are described.

Page 38, Table 3: Compound 36
Page 38, Table 4: Compound 72
Page 40, Table 6: Compound 156
Page 40, Table 7: Compound 192
Page 42, Table 9: Compound 276

Accordingly, addition of "-OCH_2O-, or -(CH=CH-CH=CH)-" is sufficiently supported by these descriptions.

(3) The support for the addition of "R^2 also represents -OCH_2O- or -(CH=CH-CH=CH)-, wherein -OCH_2O- means a methylenedioxy group and -(CH=CH-CH=CH)- means a naphthyl group together with the adjacent benzene ring." into page 11 is as follows.

It is described at page 35, lines 17-20 that "a compound in which R^2 is 3,4-(CH=CH-CH=CH) represents a 2-naphthyl group together with the adjacent benzene ring, and OCH_2O represents methylenedixoy group."

(4) The support for the addition of "The substituent R^2 on the anilino group in the formula (I) represents one or a plural number of groups (e.g., "3,5-Me" means "3,5-dimethyl")." into page 11 is as follows.

The following compounds are described.

Page 37, Table 2: Examples 7, 10, 14
Page 38, Table 3: Compound 31, 32, 33
Page 38, Table 4: Compound 68, 69
Page 40, Table 6: Compound 151, 152, 153
Page 40, Table 7: Compound 188, 189
Page 42, Table 9: Compound 271, 272, 273
Page 42, Table 10: Compound 307, 308, 309

In these compounds, R^2 is 3,5-Me, 3,5-MeO, 3,5-Cl, 3,5-Br, or 3,5-F. In this regard, it is explained at page 35, lines 4-7 that "the number before ... For example, 3,5-Me indicates 3,5-dimethyl". Based on the Examples and this description, it is originally disclosed that R^2 means one or a plural number of groups.

Respectfully submitted,

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Date: December 10, 2001

APPENDIX

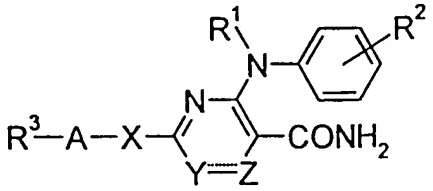
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification is changed as follows:

Page 6, first full paragraph

Namely, the invention relates to a novel heterocyclecarboxamide derivative represented by the following general formula (I) or a pharmaceutically acceptable salt thereof, and a medicament comprising the same as the active ingredient.



(I)

(wherein the symbols in the formula have the following meanings.

A: a lower alkylene which may have substituent(s), an arylene which may have substituent(s), a heteroarylene which may have substituent(s), a cycloalkylene which may have substituent(s), or H;

X: NR^4, $CONR^4$, NR^4CO, O, or S;

a dotted line between Y and Z: presence (Y=Z) or absence (Y-Z) of a bond;

Y-Z: $N(R^5)$-C(O), C(O)-$N(R^5)$, $N(R^5)$-$N(R^5)$, or C(O)-C(O);

Y=Z: N=$C(R^6)$, $C(R^7)$=N, N=N, or $C(R^7)$=$C(R^7)$;

R^1, R^4: H, a lower alkyl, -CO-lower alkyl, or -SO_2-lower alkyl;

R^2: H, a lower alkyl, a halogen, a lower alkyl substituted by halogen(s), -O-lower alkyl, -S-lower alkyl, -O-aryl, -O-lower alkylene-aryl, -S-lower alkylene-aryl, nitro, ~~or~~ cyano, ~~group~~ -OCH_2O-, or -(CH=CH-CH=CH)-;

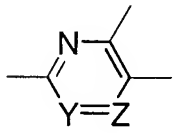
R^3: $-CO_2H$, $-CO_2$-lower alkyl, -lower alkylene-CO_2H, -lower ~~alylene~~alkylene-CO_2-lower alkyl, -CONHOH, -CONHO-lower alkyl, -lower alkylene-CONHOH, -lower alkylene-CONHO-lower alkyl, $-NH_2$, -(NH_2 in a prodrug form), -lower alkylene-NH_2, or -lower alkylene-(NH_2 in a prodrug form);

R^5: H or a lower alkyl group;

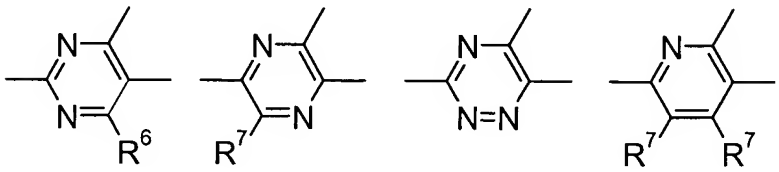
R^6: a lower alkyl, -OH, -O-lower alkyl, -O-aryl which may have substituent(s), -O-lower alkylene-aryl which may have substituent(s), $-NR^1$-aryl which may have substituent(s), -CO-lower alkyl, or -aryl group which may have substituent(s);

R^7: the same or different, H or the same group as R^6. The same shall apply to the following).

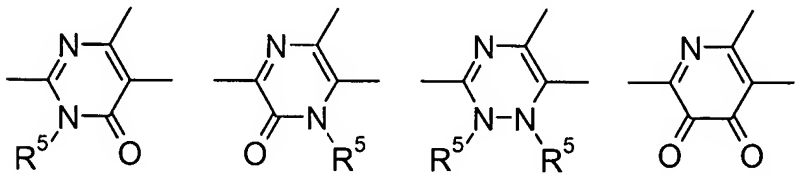
By the way, when Y=Z represents N=C(R^6), C(R^7)=N, N=N, or C(R^7)=C(R^7) in the formula, the central heterocycle part:



represents any of the following formulae:



and when Y-Z represents N(R^5)-C(O), C(O)-N(R^5), N(R^5)-N(R^5), or C(O)-C(O) in the formula, the central heterocycle part represents any of the following formulae.



Page 23, first full paragraph

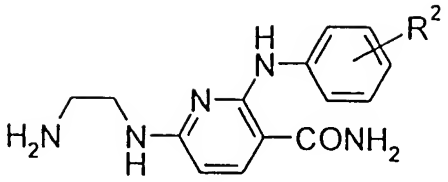
A peptide of 18 amino acid residues (MEELQDDYEDMMEENLEQ) (~~Sequence No.:~~ 1EQ ID NO:1) containing Tyr-8 of human erythrocyte Band 3 (Harrison, M. L. et al., J. Biol. Chem., 269: 955-959 (1994)) was synthesized using a peptide synthesizer. Using a biotinylation kit manufactured by Pierce, the N-terminal of the peptide in a resin-linked state was biotinylated, and purification was carried out using an HPLC.

Page 35, second full paragraph

Rex: Reference Example number, Ex: Example number, Cmpd: compound number, Ph: phenyl, Me: methyl, Et: ethyl, tBu: tert-butyl, Boc: tBuO-CO-, Bn: benzyl, Ac: acetyl, BCA: cis-2-(tert-butoxycarbonylamino)cyclohexylamino, PEA: (1'S,1R,2S)-2-(1'-phenylethylamino)cyclohexylamino, CCA: cis-2-aminocyclohexylamino, ACA: (1R,2S)-2-aminocyclohexylamino. Sal: salt (blank space: free form; HCl: hydrochloride), Dat: physicochemical data (F: FAB-MS $(M+H)^+$; FN: FAB-MS $(M-H)^-$; M: melting point (°C); A: specific rotation $[\alpha]_D$ (MeOH)). Also, a compound in which R^2 is 3,4-$(CH)_4$=CH-CH=CH). represents a 2-naphthyl group together with the adjacent benzene ring, and OCH_2O represents methylenedioxy group.

Page 38, Table 3

Table 3

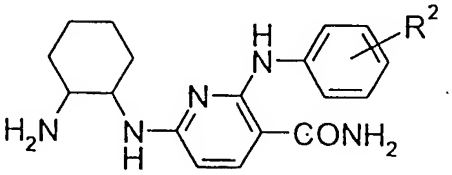


Cmpd	R^2	Cmpd	R^2	Cmpd	R^2	Cmpd	R^2
1	2-Br	10	2-H_2N	19	2-PhO	28	2-Bu
2	3-Br	11	3-H_2N	20	3-PhO	29	3-Bu
3	4-Br	12	4-H_2N	21	4-PhO	30	4-Bu
4	2-Cl	13	2-Ac	22	2-MeO	31	3,5-Cl
5	3-Cl	14	3-Ac	23	3-MeO	32	3,5-MeO
6	4-Cl	15	4-Ac	24	4-MeO	33	3,5-Me
7	2-$HOCH_2$	16	2-MeS	25	2-Me	34	2,3-OCH_2O
8	3-$HOCH_2$	17	3-MeS	26	3-Me	35	3,4-OCH_2O
9	4-$HOCH_2$	18	4-MeS	27	4-Me	36	~~3,4-(CH)$_4$~~

3.4-(CH=CH-CH=CH)

Page 38, Table 4

Table 4

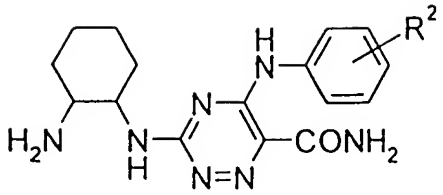


Cmpd	R^2	Cmpd	R^2	Cmpd	R^2	Cmpd	R^2
37	2-Br	46	2-H_2N	55	2-PhO	64	3-Et
38	3-Br	47	3-H_2N	56	3-PhO	65	4-Et
39	4-Br	48	4-H_2N	57	4-PhO	66	3-Pr
40	2-Cl	49	2-Ac	58	2-MeO	67	3-Bu
41	3-Cl	50	3-Ac	59	3-MeO	68	3,5-Cl
42	4-Cl	51	4-Ac	60	4-MeO	69	3,5-MeO
43	2-$HOCH_2$	52	2-MeS	61	2-Me	70	2,3-OCH_2O
44	3-$HOCH_2$	53	3-MeS	62	4-Me	71	3,4-OCH_2O
45	4-$HOCH_2$	54	4-MeS	63	2-Et	72	~~3,4-(CH)$_4$~~

3.4-(CH=CH-CH=CH)

Page 40, Table 6

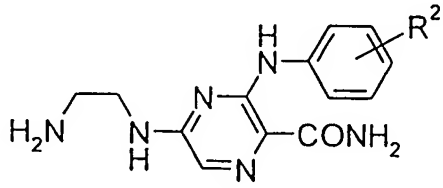
Table 6



Cmpd	R^2	Cmpd	R^2	Cmpd	R^2	Cmpd	R^2
121	2-Br	130	2-H_2N	139	2-PhO	148	2-Et
122	3-Br	131	3-H_2N	140	3-PhO	149	3-Et
123	4-Br	132	4-H_2N	141	4-PhO	150	4-Et
124	2-Cl	133	2-Ac	142	2-MeO	151	3,5-Cl
125	3-Cl	134	3-Ac	143	3-MeO	152	3,5-MeO
126	4-Cl	135	4-Ac	144	4-MeO	153	3,5-Me
127	2-$HOCH_2$	136	2-MeS	145	2-Me	154	2,3-OCH_2O
128	3-$HOCH_2$	137	3-MeS	146	3-Me	155	3,4-OCH_2O
129	4-$HOCH_2$	138	4-MeS	147	4-Me	156	~~3,4-(CH)$_4$~~ 3,4-(CH=CH-CH=CH)

Page 40, Table 7

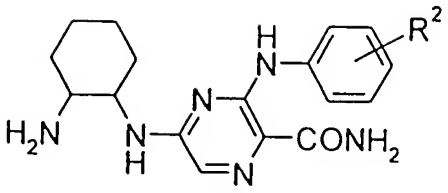
Table 7



Cmpd	R^2	Cmpd	R^2	Cmpd	R^2	Cmpd	R^2
157	2-Br	166	2-$HOCH_2$	175	2-MeS	184	4-Me
158	3-Br	167	3-$HOCH_2$	176	3-MeS	185	2-Et
159	4-Br	168	4-$HOCH_2$	177	4-MeS	186	3-Et
160	2-Cl	169	2-H_2N	178	2-PhO	187	4-Et
161	3-Cl	170	3-H_2N	179	3-PhO	188	3,5-MeO
162	4-Cl	171	4-H_2N	180	4-PhO	189	3,5-Me
163	2-F	172	2-Ac	181	2-MeO	190	2,3-OCH_2O
164	3-F	173	3-Ac	182	4-MeO	191	3,4-OCH_2O
165	4-F	174	4-Ac	183	2-Me	192	~~3,4-(CH)$_4$~~ 3,4-(CH=CH-CH=CH)

Page 42, Table 9

Table 9

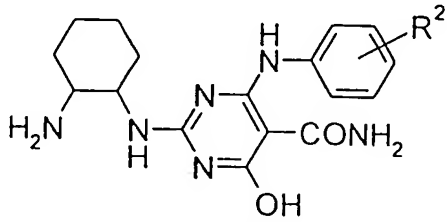


Cmpd	R^2	Cmpd	R^2	Cmpd	R^2	Cmpd	R^2
241	2-Br	250	2-H_2N	259	2-PhO	268	2-CN
242	4-Br	251	3-H_2N	260	4-PhO	269	3-CN
243	2-Cl	252	4-H_2N	261	2-MeO	270	4-CN
244	4-Cl	253	2-Ac	262	4-MeO	271	3,5-Br
245	2-F	254	3-Ac	263	2-Et	272	3,5-Cl
246	4-F	255	4-Ac	264	4-Et	273	3,5-F
247	2-$HOCH_2$	256	2-MeS	265	2-NO_2	274	2,3-OCH_2O
248	3-$HOCH_2$	257	3-MeS	266	3-NO_2	275	3,4-OCH_2O
249	4-$HOCH_2$	258	4-MeS	267	4-NO_2	276	~~3,4-(CH)$_4$~~

Page 42, Table 10

3,4-(CH·CH-CH·CH)

Table 10



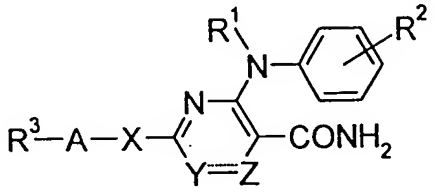
Cmpd	R^2	Cmpd	R^2	Cmpd	R^2	Cmpd	R^2
277	2-F	286	2-H_2N	295	2-PhO	304	2-Bu
278	3-F	287	3-H_2N	296	3-PhO	305	3-Bu
279	4-F	288	4-H_2N	297	4-PhO	306	4-Bu
280	2-Cl	289	2-Ac	298	2-MeO	307	3,5-Cl
281	3-Cl	290	3-Ac	299	3-MeO	308	3,5-MeO
282	4-Cl	291	4-Ac	300	4-MeO	309	3,5-Me
283	2-$HOCH_2$	292	2-MeS	301	2-Et	310	2,3-OCH_2O
284	3-$HOCH_2$	293	3-MeS	302	3-Et	311	3,4-OCH_2O
285	4-$HOCH_2$	294	4-MeS	303	4-Et	312	~~3,4-(CH)$_4$~~

3,4-(CH:CH-CH:CH)

IN THE CLAIMS:

The claims are amended as follows:

1. (Amended) A heterocyclecarboxamide derivative represented by the general formula (I) or a salt thereof.



(I)

wherein the symbols in the formula have the following meanings:

A: a lower alkylene which may have substituent(s), an arylene which may have substituent(s), a heteroarylene which may have substituent(s), or a cycloalkylene which may have substituent(s);

X: NR^4, $CONR^4$, NR^4CO, O, or S;

a dotted line between Y and Z: presence (Y=Z) or absence (Y-Z) of a bond;

Y-Z: $N(R^5)$-C(O), C(O)-$N(R^5)$, $N(R^5)$-$N(R^5)$, or C(O)-C(O);

Y=Z: N=$C(R^6)$, $C(R^7)$=N, N=N, or $C(R^7)$=$C(R^7)$;

R^1, R^4: H, a lower alkyl, -CO-lower alkyl, or -SO_2-lower alkyl;

R^2: H, a lower alkyl, a halogen, a lower alkyl substituted by halogen(s), -O-lower alkyl, -S-lower alkyl, -O-aryl, -O-lower alkylene-aryl, -S-lower alkylene-aryl, nitro, ~~or~~ cyano, ~~group~~ -OCH_2O-, or -(CH=CH-CH=CH)-;

R^3: -CO_2H, -CO_2-lower alkyl, -lower alkylene-CO_2H, -lower ~~alylene~~alkylene-CO_2-lower alkyl, -CONHOH, -CONHO-lower alkyl, -lower alkylene-CONHOH, -lower alkylene-CONHO-lower alkyl, -NH_2, -(NH_2 in a prodrug form), -lower alkylene-NH_2, or -lower alkylene-(NH_2 in a prodrug form);

R^5: the same or different, H or a lower alkyl group;

R^6: a lower alkyl, -OH, -O-lower alkyl, -O-aryl which may have substituent(s), -O-lower alkylene-aryl which may have substituent(s), -NR^1-aryl which may have substituent(s), -CO-lower alkyl, or -aryl group which may have substituent(s); and

R^7: the same or different, H or the same group as R^6.